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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,829	07/14/1999	PATRICK M SCHLIEVERT	600.347USWO	6703

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EXAMINER

HINES, JANA A

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 09/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/308,829

Applicant(s)

SCHLIEVERT ET AL.

Examiner

Ja-Na Hines

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-27,35-37 and 45-99 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-27,35-37 and 45-99 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Amendment Entry

1. Amendments have been entered as filed on May 27, 2003. Amendment to the specification is acknowledged. Claims 24-27, 35-37 and 45-67 have been amended. Claims 28-34 and 38-44 have been cancelled. Claims 48-99 have been newly added. Claims 24-27, 35-37 and 45-99 are under consideration in this office action.

Withdrawal of Rejections

2. The following rejections have been withdrawn in view of applicants' amendments and arguments:

a) The enablement rejection of claims 24-44, 53 and 57-67 under 35 U.S.C. 112 first paragraph.

Response to Amendment

3. Applicant's arguments with respect to claims 24-27, 35-37 and 45-99 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 24-27, 35-37 and 45-99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to polypeptides comprising substitutions at more than one of the amino acids and exotoxin polypeptides with at least 97.5% identity to SEQ ID NO:2.

The specification broadly describes an exotoxin that has at least one change wherein the change can be an amino acid substitution, deletion or addition. The specification goes on to recite that the change should minimize the reversion of the mutant having systemic lethality or toxicity. It is preferred that the change does not result in a change of the toxin's ability to stimulate an antibody response. See the instant specification pages 8-9. The specification teaches specific amino acid substitutions at amino acid positions 12, 15, 17, 35 and 38 of SEQ ID NO:2. Thus the written description in this case only sets forth the specifically recited amino acid substitutions and not the fully breadth of the claims. i.e., any polypeptides with at least 97.5% identity to SEQ ID NO:2; therefore the written description is not commensurate in scope with the claims.

There must be some nexus between the structure of the protein encoded and that function of that protein. However, function cannot be predicted from the modification of the structure of the polypeptide. Without any limitation on the sequence identity besides the percent identity, the

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sequence fails to have an adequate written description. The specification fails to teach variants outside of the specifically named amino acid substitutions. There are no teachings of sequences with amino acids additions or deletions, yet the claims encompass such. Furthermore, there is no description within the specification that the claimed polypeptides exist independent of the function, i.e., being mutant SPE-C toxins. The specification fails to teach the structure or relevant identifying characteristics of such polypeptides.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically identified amino acid substitutions, the skilled artisan cannot envision the detailed structure of the claimed exotoxin polypeptides, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus.

Sequences having 97.5% identity to either SEQ ID NO:2 fail to meet the written description provision of 35 UCS 112, first paragraph. Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, make clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). The specification discloses SEQ ID NO: 2 with specific amino acid substitutions, there is no disclosure of generic sequences with 97.5% identity to SEQ ID NO: 2 which are comprised in the family of mutant toxin polypeptides. Thus, the structure of these polypeptides is not defined. Even though the claims recite at least one amino acid change, the claims do not teach what the other additions, substitutions or deletions. The claims do not limit the substitutions to the recited positions. Thus, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides since the specification has not defined what the variables can be. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method for determining sequence identity. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression.

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by

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showing that the invention was “ready for patenting” such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by “whatever characteristics sufficiently distinguish it”). The instant specification does not describe the claimed invention sufficient to show that the applicant was in possession of the claimed invention.

Currently the claims are insufficient to support the claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph.


5. Claims 24-26, 35-37 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular claims 24-25, 35-36 and 59 refer to substitution at more than one of these amino acids. However it is unclear if these amino acids refer to the amino acids comprised in SEQ ID NO:2 or are limited to only the specifically named amino acid substitutions. Therefore clarification is required to overcome the rejection.

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6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines 
August 25, 2003


LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600